retinoblastoma

Retinoblastoma is a rare type of eye cancer that usually develops in early childhood, typically before the age of 5. This form of cancer develops in the retina, which is the specialized light-sensitive tissue at the back of the eye that detects light and color.

In most children with retinoblastoma, the disease affects only one eye. However, one out of three children with retinoblastoma develops cancer in both eyes. The most common first sign of retinoblastoma is a visible whiteness in the pupil called "cat's eye reflex" or leukocoria. This unusual whiteness is particularly noticeable in photographs taken with a flash. Other signs and symptoms of retinoblastoma include crossed eyes or eyes that do not point in the same direction (strabismus); persistent eye pain, redness, or irritation; and blindness or poor vision in the affected eye(s).

Retinoblastoma is often curable when it is diagnosed early. However, if it is not treated promptly, this cancer can spread beyond the eye to other parts of the body. This advanced form of retinoblastoma can be life-threatening.

When retinoblastoma is associated with a gene mutation that occurs in all of the body's cells, it is known as germinal retinoblastoma. People with this form of retinoblastoma also have an increased risk of developing several other cancers outside the eye. Specifically, they are more likely to develop a cancer of the pineal gland in the brain (pinealoma), a type of bone cancer known as osteosarcoma, cancers of soft tissues such as muscle, and an aggressive form of skin cancer called melanoma.

Frequency

Retinoblastoma is diagnosed in 250 to 350 children per year in the United States. It accounts for about 4 percent of all cancers in children younger than 15 years.

Genetic Changes

Mutations in the *RB1* gene are responsible for most cases of retinoblastoma. *RB1* is a tumor suppressor gene, which means that it normally regulates cell growth and keeps cells from dividing too rapidly or in an uncontrolled way. Most mutations in the *RB1* gene prevent it from making any functional protein, so it is unable to regulate cell division effectively. As a result, certain cells in the retina can divide uncontrollably to form a cancerous tumor. Some studies suggest that additional genetic changes can influence the development of retinoblastoma; these changes may help explain variations in the development and growth of tumors in different people.

A small percentage of retinoblastomas are caused by deletions in the region of chromosome 13 that contains the *RB1* gene. Because these chromosomal changes

involve several genes in addition to *RB1*, affected children usually also have intellectual disability, slow growth, and distinctive facial features (such as prominent eyebrows, a short nose with a broad nasal bridge, and ear abnormalities).

Inheritance Pattern

Researchers estimate that 40 percent of all retinoblastomas are germinal, which means that *RB1* mutations occur in all of the body's cells, including reproductive cells (sperm or eggs). People with germinal retinoblastoma may have a family history of the disease, and they are at risk of passing on the mutated *RB1* gene to the next generation. The other 60 percent of retinoblastomas are non-germinal, which means that *RB1* mutations occur only in the eye and cannot be passed to the next generation.

In germinal retinoblastoma, mutations in the *RB1* gene appear to be inherited in an autosomal dominant pattern. Autosomal dominant inheritance suggests that one copy of the altered gene in each cell is sufficient to increase cancer risk. A person with germinal retinoblastoma may inherit an altered copy of the gene from one parent, or the altered gene may be the result of a new mutation that occurs in an egg or sperm cell or just after fertilization. For retinoblastoma to develop, a mutation involving the other copy of the *RB1* gene must occur in retinal cells during the person's lifetime. This second mutation usually occurs in childhood, typically leading to the development of retinoblastoma in both eyes.

In the non-germinal form of retinoblastoma, typically only one eye is affected and there is no family history of the disease. Affected individuals are born with two normal copies of the *RB1* gene. Then, usually in early childhood, both copies of the *RB1* gene in retinal cells acquire mutations or are lost. People with non-germinal retinoblastoma are not at risk of passing these *RB1* mutations to their children. However, without genetic testing it can be difficult to tell whether a person with retinoblastoma in one eye has the germinal or the non-germinal form of the disease.

Other Names for This Condition

- Glioma, retinal
- RB

Diagnosis & Management

These resources address the diagnosis or management of retinoblastoma:

- GeneReview: Retinoblastoma
  https://www.ncbi.nlm.nih.gov/books/NBK1452
- Genetic Testing Registry: Retinoblastoma
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C0035335/

- Genomics Education Programme (UK)
  https://www.genomicseducation.hee.nhs.uk/resources/genetic-conditions-factsheets/item/85-retinoblastoma
- MedlinePlus Encyclopedia: Retinoblastoma
  https://medlineplus.gov/ency/article/001030.htm
- National Cancer Institute: Genetic Testing for Hereditary Cancer Syndromes
  https://www.cancer.gov/about-cancer/causes-prevention/genetics/genetic-testing-fact-sheet

These resources from MedlinePlus offer information about the diagnosis and management of various health conditions:

- Diagnostic Tests
  https://medlineplus.gov/diagnostictests.html
- Drug Therapy
  https://medlineplus.gov/drugtherapy.html
- Surgery and Rehabilitation
  https://medlineplus.gov/surgeryandrehabilitation.html
- Genetic Counseling
  https://medlineplus.gov/geneticcounseling.html
- Palliative Care
  https://medlineplus.gov/palliativecare.html

Additional Information & Resources

MedlinePlus

- Encyclopedia: Retinoblastoma
  https://medlineplus.gov/ency/article/001030.htm
- Health Topic: Eye Cancer
  https://medlineplus.gov/eyecancer.html
- Health Topic: Retinal Disorders
  https://medlineplus.gov/retinaldisorders.html

Genetic and Rare Diseases Information Center

- Retinoblastoma
  https://rarediseases.info.nih.gov/diseases/7563/retinoblastoma

Additional NIH Resources

- National Cancer Institute
  https://www.cancer.gov/types/retinoblastoma
- National Eye Institute
  https://nei.nih.gov/health/retinoblastoma/

Educational Resources

- Boston Children's Hospital
  http://www.childrenshospital.org/conditions-and-treatments/conditions/retinoblastoma
- Cleveland Clinic
  http://my.clevelandclinic.org/health/articles/retinoblastoma
- Digital Journal of Ophthalmology
  http://www.djo.harvard.edu/site.php?url=/patients/pi/436#
- Disease InfoSearch: Retinoblastoma
  http://www.diseaseinfosearch.org/Retinoblastoma/6282
- KidsHealth from the Nemours Foundation
  http://kidshealth.org/en/parents/retinoblastoma.html
- MalaCards: retinoblastoma
  http://www.malacards.org/card/retinoblastoma
- Merck Manual Consumer Version
  http://www.merckmanuals.com/home/children-s-health-issues/childhood-cancers/retinoblastoma
- My46 Trait Profile
  https://www.my46.org/trait-document?trait=Retinoblastoma&type=profile
- Orphanet: Retinoblastoma
  http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=790

Patient Support and Advocacy Resources

- American Cancer Society
  http://www.cancer.org/cancer/retinoblastoma.html
- American Childhood Cancer Organization
  http://www.acco.org/
- CureSearch (the Children's Oncology Group and the National Childhood Cancer Foundation)
  http://curesearch.org/Retinoblastoma-in-Children

- National Organization for Rare Disorders (NORD)
  https://rarediseases.org/rare-diseases/retinoblastoma/
- Resource list from the University of Kansas Medical Center
  http://www.kumc.edu/gec/support/retinobl.html
- The EyeCare Foundation
  http://www.eyecancercure.com/

GeneReviews

- Retinoblastoma
  https://www.ncbi.nlm.nih.gov/books/NBK1452

Genetic Testing Registry

- Retinoblastoma
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C0035335/

ClinicalTrials.gov

- ClinicalTrials.gov
  https://clinicaltrials.gov/ct2/results?cond=%22retinoblastoma%22

Scientific articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28Retinoblastoma%5BMAJR%5D%29+AND+%28retinoblastoma%5BTI%5D%29+AND+review%5Bpt%5D+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D

OMIM

- RETINOBLASTOMA
  http://omim.org/entry/180200

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